

ETHICAL DECISION-MAKING UNDER RADICAL UNCERTAINTY

by

Hunter Jackson Smith, MD, MPH

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Abstract

We live in a world of ever-increasing knowledge and dissemination of data. This information can provide us with new concepts or associations which may hold significant implications for how we approach problems. However, we must be cautious in how we appraise such information. There are circumstances in which tenuous epistemologic linkages or hints of burgeoning concepts lead to heavy overestimation in our deliberations and actions, which may negatively impact the ways in which individuals behave and policymakers legislate. It is therefore becoming increasingly important to take account of how we ought to evaluate new information. We must derive a structured, systematic approach to how we weigh different forms and levels of evidence within our deliberative processes. In the face of radical uncertainty and shaky epistemologic foundations, there manifests ethical responsibilities with two normative claims: ethically responsible deliberation and ethical action in response to the deliberation. This thesis offers a novel framework for the ethical evaluation of evidence in decision-making based upon an appraisal of the strength of evidence and magnitude of impact of a given situation – the Evidence Appraisal & Actionability Tool. The tool further purports an ethical actionability depending upon the grade. One example of its application to a newly forming scientific concept – the potential interactions between the gut microbiome, livestock, and human obesity – illustrates its utility and interpretation. Ultimately, the value offered by this Evidence Appraisal & Actionability Tool is in its ability to provide guidance for how one ought to incorporate existing information into one’s decision-making in an ethically appropriate fashion, regardless of context or circumstance, and how one ought to act in response to such evidence.

Primary Reader – Gail Geller, ScD, MHS

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I. Introduction

We live in a world of ever-increasing knowledge and dissemination of data. This information can provide us with new concepts or associations which may hold significant implications for how we approach problems. However, we must be cautious in how we appraise such information. There are circumstances in which tenuous epistemologic linkages or hints of burgeoning concepts lead to heavy overestimation in our deliberations and actions, which may negatively impact the ways in which individuals behave and policymakers legislate. It is therefore becoming increasingly important to take account of how we ought to evaluate new information.

We must derive a structured, systematic approach towards how we weigh different forms and levels of evidence within our deliberative process. In the face of radical uncertainty and shaky epistemologic foundations, there manifests ethical responsibilities in how we approach and weigh information, the ethical implications between the deliberative and action processes, and in the consequences yielded from the actions taken based upon the deliberations. It implies both an ethics of process as well as consequence. Thus, there are two normative claims: ethically responsible deliberation and ethical action in response to the deliberation. This thesis offers a novel framework for the evaluation of evidence in ethical decision-making based upon an appraisal of the strength of evidence and magnitude of impact of a given situation. It then provides an example of its application to a newly forming scientific concept – the potential interactions between the gut microbiome, livestock, and human obesity. Ultimately, the value offered by this Evidence Appraisal & Actionability Tool is in its ability to provide guidance for how one ought to incorporate existing information into one's decision-making in an ethically

appropriate fashion, regardless of context or circumstance, and how one ought to act in response to such evidence.

II. Background

There is uncertainty underlying the data that informs our decisions. One can posit that a person can never be 100 percent certain that the action they perform will result in its intended consequence. This is an idea David Hume discusses in his concepts of “relations of ideas” and “matters of fact” in *An Enquiry into Human Understanding* (Hume, 1779). “Relations of ideas” concern topics such as logic and mathematics where the premises and conclusions are objectively demonstrable, 100 percent predictable, and proven by reason *a priori*. An example of this is the proposal that the angles of a Euclidean triangle will always sum to 180 degrees. This is knowledge that remains true regardless of whether it is found in nature. This is in contrast to “matters of fact,” which he defines as forms of knowledge relying upon cause and effect relationships determined through experience and induction. As such, the process of inductive inferences from previous observations of cause and effect implies that there always remains a possibility of a resulting expected effect being expectation-dystonic from the observed cause. For example, one could drop a pencil with the expectation of it hitting the ground. One has witnessed the cause-effect relationship between dropping objects and gravity thousands of times in the past, so one has near 100 percent certainty this will be the result again. Yet it is possible that a stray ripple through spacetime could force its way through the expected dropped pencil’s path to propel it towards the ceiling. This may be an extreme example but is intended to illustrate the idea that even in circumstances in which we have a tremendous amount of certainty in the data which informs our decisions, there is always an underlying degree of uncertainty. Thus, at one

extreme end of uncertainty, we can point out that all empirical claims are uncertain; yet there are certainly relative differences in degrees of uncertainty, so we must decide when that uncertainty impedes action.

This concept of ambiguity surrounding the data informing our decisions is particularly important in cases of radical uncertainty. What do we mean when we say “radical uncertainty”? It is the phenomenon in which there is a considerable amount of ambiguity or lack of solid clarity regarding the evidence for a situation. Yet, practically speaking, it is the case that regardless of the level of certainty of the data we have before us, we must act with what existing evidence we have. For example, there may hypothetically be a new study released demonstrating a potential association between cat ownership and pancreatic cancer. However, there may only be only a small handful of studies even considering this issue with a great deal of uncertainty regarding the accuracy of the claim. Regardless, we must decide how we ought to approach this potential issue of cats and pancreatic cancer from a public health perspective. Shall we make a uniform policy banning cats from households? Will we relay public warnings of the dangers of cats and cancer? Or should we not act upon this data?

In this example, it seems obvious the correct approach would be to give very little weight to these proposed associations and appropriately decide not to act upon this tenuous evidence. However, this is not always the case. We could replace cat ownership with any myriad of potential exposures (e.g. sugar consumption), and it could elicit a more distressing issue of radical uncertainty. It is therefore also important to determine what the obligation to action is in response to newfound information with respect to research, behavior, policy, etc. It would be inappropriate to invest time and resources into a highly suspect idea (e.g. cat exposure and pancreatic cancer) due to the detraction as an opportunity cost. Yet there are other newly

presented concepts which are more plausible with similar levels of evidential uncertainty that may warrant further investigation (e.g. sugar consumption and pancreatic cancer). Thus, there appears to be a difference between credible radical uncertainty and implausible radical uncertainty.

It is important to also differentiate radical uncertainty from speculative ethics, which examines ethical concerns that arise from hypothetical future contexts (Schick, 2016). For example, a speculative concern might address the potential for future nanotechnologies to wipe out an entire species and discuss the ethics of how we ought to approach nanotechnology both now and in the future. This is also to differentiate radical uncertainty from general uncertainty, in which ethical ideas such as decision theory, utilitarianism, and the precautionary principle come into play. Radical uncertainty must be considered as a distinct concept and one which holds increasingly greater importance in our world.

How we weigh and consider the data and information available to us is necessarily an ethical pursuit. When attempting to act on the basis of evidence, we weigh the evidence available to us and choose the path that we judge most likely, based on the evidence, to bring about the desired outcome. How we make decisions and take actions with ethical impacts – whether because it brings about harms or benefits, leads to rights violations or injustice, etc. – is necessarily an ethical pursuit. Thus, we have an ethical impetus to appropriately weigh data and information in our decision-making.

We live in a suboptimal data and evidence world. If we had knowledge of all of the causal factors underlying consequences or natural manifestations we observe in addition to the exact cause-effect impacts of our actions, we would live an optimal evidence environment. However, we are presented with problems every day at individual and population levels which

require us to act either responsively or preemptively under varying degrees of uncertainty regarding the causes of the problems and the relationship between our actions and intended consequences. If one were to make decisions based upon shaky evidence, then one would be taking a risk. If those decisions held ethical impacts, then that decision-making process could be deemed ethically shaky from a consequences and/or process perspective.

One clear example of this comes from the world of preventive medicine and public health through the United States Preventive Services Task Force (USPSTF) recommendations. The USPSTF's job is to offer standard of care recommendations for preventive interventions for all primary care providers based upon available evidence. For example, the USPSTF recommends that all women who are planning on or capable of becoming pregnant take daily folic acid supplementation to avoid potential neural tube defects in a developing fetus (USPSTF, 2017). They take a particularly scrutinizing eye to the existing data regarding a health care service and disease outcome to arrive at their judgments. Sometimes they change their recommendations based upon new studies that add more perspective to the literature. However, there are situations in which the evidence is still weak or new, yet they must still come to a decision as to how to value this information and what they will recommend based upon it. The USPSTF therefore developed a grading scheme for their recommendations and categorize them according to their level of certainty regarding the data and its potential effects (USPSTF, 2018):

Figure 1: USPSTF Recommendation Grades

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

The USPSTF is therefore forced into the position where they must make decisions that may have substantial health and ethical impacts on millions of patients but where there is considerable uncertainty underlying the data on which they base their recommendations. For the USPSTF, an “I” grade constitutes radical uncertainty in that the potential screening or prevention modality is credible enough to be worth assessing, yet there is an insufficient level of confidence regarding the harms and benefits. Since their recommendations impact millions of patients and are geared towards preventive measures, their threshold for certainty and confidence in the data is much higher than might be considered in other contexts. Thus, they neither recommend nor recommend against the practice in question if it is judged to be grade “I”. They instead leave it to the discretion of the provider with the stipulation they convey the uncertainty of the data to the patient. Further, they do not provide guidance or actionability regarding the next steps related to “I” grades for the medical or research community as a whole.

How we ought to approach data increases in difficulty under conditions of radical uncertainty. Considerable levels of uncertainty leave us much less confident in how we should proceed, and we must think through this process. We are confronted by an ever-growing front of new pieces of information and associative linkages which must be accounted for in our deliberations. Yet there is not an existing evidence appraisal method which links ethical obligations and actionability. Therefore, we require a framework for thinking about radical uncertainty and how we weigh various levels of information confidence into our ethical decision-making. Further, we need a method for determining what level of uncertainty we currently are in for a given subject, and what ethical responsibility we have in how we ought to weigh that information in light of that determined level.

III. An Approach to the Consideration of Information

There are two appraisal components to the Evidence Appraisal & Actionability Tool: strength of evidence and magnitude of impact. First, we must make an assessment regarding the strength of evidence. This represents the level of certainty we have regarding the information at hand. There are several conceptual measures which contribute to this criterion. One grouping of concepts is Hill's criteria for causality, which includes a set of nine areas that contribute to an epidemiologic conclusion for a causal relationship between a cause and effect. It includes strength, reproducibility, specificity, temporality, biological gradient, plausibility, coherence, experimental evidence, and analogy (Hill, 1965). Though some of these concepts do not apply to every context (e.g. biological gradient), they provide a useful guide in asserting which criteria we ought to value in considering our strength of evidence. One may also turn to other existing frameworks, such as the USPSTF's levels of uncertainty, other epidemiologic concepts (e.g.

validity, generalizability), etc. for more input into guiding how one ought to frame data and information. The key ideas inherent to the strength of evidence component include our level of confidence in the data presented to us, which relies upon other underlying concepts such as quality and trustworthiness of the research. Once we have assessed the available information per these values for strength of evidence, we must then categorize it as Strong, Moderate, or Weak.

After we have completed this first step, we must then consider the magnitude of impact. The conceptual measures for the magnitude of impact may vary depending upon which context one is applying the tool. However, for a public health-based consideration, potential concepts might include morbidity, mortality, quality of life, economic impact, etc. One must consider various distributions of impact as well, as they may be equivalent in different ways – e.g. an enormous impact on a small number of people vs a small impact in a large number of people might both be categorized similarly. The idea underlying the magnitude of impact component is that we must consider the entire scope of magnitude and effects incurred by the information being appraised. Once it has been assessed, we must then categorize it as Substantial, Moderate, or Minimal.

Upon full assessment and consideration of the strength of evidence and magnitude of impact, one must then categorize the data utilizing the Evidence Appraisal & Actionability Tool, as illustrated below:

Figure 2: The Evidence Appraisal & Actionability Tool

		Strength of Evidence		
Magnitude of Impact		Strong	Moderate	Weak
	Substantial	A	B	C1
	Moderate	B	B	D
	Minimal	C2	D	F

The Evidence Appraisal & Actionability Tool provides grades for the data one is assessing based upon these measures of evidence and impact. Its value is derived from its ability to provide guidance concerning the ethical responsibilities of how one ought to proceed regarding their decision-making in light of available information and approaching such data. The guidance varies depending upon its grading categorization and yields the following conclusions:

Grading:

- A = One must incorporate this data in deliberations and consider it trustworthy.
- B = One ought to strongly consider this data in deliberations and consider it trustworthy.
- C = This data ought to be considered on a case-by-case basis.
- Weak Evidence, Substantial Magnitude (C1): One should approach the data cautiously and be careful of the amount of weight placed on its results. More research is required to trust the data with greater confidence and more accurately discern its impact. Because it has the potential for a substantial magnitude of impact, there is a significant need to conduct more research on this area.

- Strong Evidence, Minimal Magnitude (C2): One should trust the data, but one should not heavily weigh it in deliberations. It may act as a contributing feature but should not lead the main discussion.
- D = There may be relevant concerns in this data, but it ought not to be considered in most cases. More research is required to accurately discern its impact with greater certainty.
- F = This data is insignificant and poorly formed; it should not be considered at all in deliberations.

There are some further considerations relevant to the use of the tool. First, it is important to clearly differentiate the Evidence Appraisal & Actionability Tool from other data evaluation tools, such as the USPSTF recommendation grades. There are differences in judgment kinds regarding who is undertaking the decision-making. For example, there is a significant difference in considering “C1” level data on nationwide policy decisions versus those made by individuals. It would be unethical and irresponsible in the vast majority of cases for one to seriously weigh and act upon C1 level data impacting thousands to millions of people. This is a weighty consideration for the USPSTF when providing guidance regarding preventive recommendations at a national level. Thus, they only make affirmative “a provider should offer this service” recommendations when there is a significant amount of evidence to support their decision. On the other hand, if an individual wanted to act upon C1 level data that impacted only him- or herself, it may be more justifiable to do so. One might ask, “Why doesn’t the Evidence Appraisal & Actionability Tool look like USPSTF’s or any other decision matrix (e.g. American College of Cardiology/American Heart Association)?” These matrices serve very particular contexts. For example, the USPSTF must specifically determine which preventive services are appropriate and should be pursued, which potentially impact millions of people. Therefore, their recommendation

decision matrix is incredibly conservative. The ACC/AHA must offer recommendations regarding treatment modalities and procedures physicians consider at the individual physician-patient level (ACC/AHA Task Force on Practice Guidelines, 2010; Halperin, et al, 2015). Their recommendations are more flexible regarding the assessment of evidence and what is considered sufficient for different levels of claims as to how physicians should act in response to such evidence. However, the Evidence Appraisal & Actionability Tool is not constrained to the public health or physician-patient dyad contexts – it may be applied across any discipline.

These other decision tools such as USPSTF's and ACC/AHA's are certainly useful, yet they are not designed to provide normative obligations or offer epistemologic guidance across disparate contexts. There are examples where epistemology is invoked in the ethical debate regarding how we ought to appraise data and what obligations we have to our actions and decision-making process based upon that data. Two prominent examples of this are climate change and vaccines. In both of these situations, they both have substantial magnitude of impact and there are very convincing data supporting its existence, and safety and efficacy, respectively. Thus, one can determine via the Evidence Appraisal & Actionability Tool that they would both be A grades - one must incorporate this data in deliberations and consider it trustworthy. However, there remain those who do not harmonize their decision-making processes and related actions with the existing evidence base for these concepts. As such, based upon the Evidence Appraisal & Actionability Tool, we may determine that those who reject the evidence supporting climate change and vaccines are acting unethically by being epistemologically irresponsible, which leads to dangerous, unethical consequences (e.g. not promoting environmentally supportive legislation; not vaccinating one's children despite lack of contraindications). Further, we can also determine that those who accept and appropriately weigh the evidence yet do not

utilize the evidence in their decision-making and actions are also acting unethically. Therefore, the frameworks are similar in that they all concern the appraisal of data and information. However, they are distinctly different in that only the Evidence Appraisal & Actionability Tool offers normative weight in how one ought to act or is even ethically obligated to act in the face of certain grades of evidence.

Second, the grading is not static; it is a dynamic process. For example, an area of data can move from D to C to B to D (or what have you) as more research and information is gained on the subject. Knowledge assurance and our consideration of it is dynamic; it is influenced as we learn more about the subject.

Third, how one considers the grading may depend upon the context due to judgments of different kinds. One criticism of the tool might argue that the demarcations between the levels for the strength of evidence and magnitude of impact are too vague and allows too much room for disagreement regarding categorization. Though this is certainly a concern, the tool must be flexible enough to apply across a variety of decision-making contexts. For example, there are different standards for evidence in engineering fields compared to social sciences. This tool could help different fields to individually determine how they wish to weigh their information via a deliberative process, though the values and gradings remain constant across disciplines.

Fourth, there is no category for when data reveals negligible or no effect. Though it might go without saying, all data of this type should be categorized with an “F” grade. One should not weigh it at all in decision-making. Similarly, if the evidence is so untenable or implausible to the extent a possibility of its veracity is remote, it should also be categorized with an “F” grade. Therefore, one can imagine a surrounding border of red “F” grades below minimal magnitude of impact and to the right of weak strength of evidence categories.

Fifth, not all evidence contexts within the same grading categorization are equal. For example, two separate contexts could both be considered grade C2 yet have differences between them. One can imagine the C2 box as a two-dimensional sliding scale with differing levels of strength of evidence and magnitude of impact even within this category. This is demonstrated graphically with the two hypothetical contexts labelled “1” and “2” as follows:

Figure 3: Example of the Two-Dimensional Sliding Scale within the Evidence Appraisal & Actionability Tool

		Strength of Evidence		
		Strong	Moderate	Weak
Magnitude of Impact	Substantial	A	B	C1
	Moderate	B	B	D
	Minimal	<div>●1</div> C2 <div>2●</div>	D	F

Context 1 illustrates a situation in which we are very confident in the evidence and there is only a minimal potential impact of the decision, action, or evidence. As such, context 1 is assuredly a C2. Yet Context 2 lies on the edge of three other categories: Strong-Moderate B, Moderate-Moderate B, and Moderate-Minimal D. Its position could quickly slide from the C2 category to B or D depending upon what future evidence is presented. Thus, even within each category, each context is different and nuanced. However, the ethical responsibility and guidance concerning that information remains the same regardless of the intra-category variation.

Sixth, the discussion of intra-category variation raises the question of why Moderate-Moderate, Strong-Moderate, and Moderate-Substantial categories are all considered Grade B recommendations. The reasoning remains the same. Although these three categories contain inherent differences between them, their overall consideration regarding their appraisal is

equivalent. Namely, although they may demonstrate these differences in character, they all warrant strong consideration in deliberations and should be considered trustworthy.

There is one final caveat to this as well, and it regards emergency circumstances. There may arise dire cases in which one absolutely must act in *some* way despite little or no evidence to substantiate one's expected action-consequence connection. Some examples might include a global response to an impending meteor impact of catastrophic magnitude, an individual's countermeasures to stave off a much more powerful malcontent, etc. Yet in each of these circumstances, the basic underlying theme remains the same – even if there is possibly little to no evidence to support one's decisions in a *must-act* situation, one must still apply the same reasoning in the tool (i.e. weighing certainty and magnitude of impact) if one wishes to act responsibly and ethically.

In summary, uncertainty often underlies the data and information we receive. However, we must nevertheless make decisions and act while relying upon varying types and degrees of uncertainty of data. These decisions and actions have ethical implications for both the user and on those they may impact. We therefore have an ethical obligation to appraise such information in a responsible way. The Evidence Appraisal & Actionability Tool offers us a method by which to fulfill this ethical responsibility. Further, it provides guidance regarding how we ought to weigh relevant information according to each grade of evidence. The next step is to apply the tool to a case study which exemplifies its use in a context of evidential radical uncertainty. A prime example of this from a public health perspective is the potential association between human-livestock microbiome transmissibility and the subsequent development of obesity, i.e. the hypothesis of a link between the hologenome and human obesity.

IV. The Hologenome and Human Obesity

A. Introduction

Humans have been omnivorous from the time we diverged as our own species from the genetic tree. Since that time, we have created increasingly more efficient ways of cultivating animals for consumption to satiate our carnivorous desires. However, we have found through empirical evidence that meat consumption incurs a multitude of negative effects for human health, animal treatment, and environmental well-being. Yet despite knowledge of these negative consequences, most of the planet continues to increase its meat consumption at an alarming rate. In order to fulfill such market demands, livestock farmers and agricultural corporations over the past century have been artificially selecting for and breeding their cash animals to be more and more metabolically efficient. Such metabolic efficiency allows them to achieve several times larger yields for the same amount of resource input. However, by artificially selecting for more metabolically efficient animals, we may have been inadvertently pushing humanity towards becoming more metabolically efficient humans. The present section will investigate the ethics of livestock artificial selection in the context of the obesity epidemic and global climate change and will demonstrate the application of the Evidence Appraisal & Actionability Tool.

B. The Hologenome, Livestock, and Obesity

Obesity is defined by the CDC as “weight that is higher than what is considered as a healthy weight for a given height,” and is multifactorial (CDC, 2016; Dhurandhar & Keith, 2014). It is a rising epidemic in the United States and across the world. Per the CDC’s National Center for Health Statistics 2015-2016 data, 71% of adults over 20 years-old in the U.S. were overweight or obese and 39.8% were obese (CDC, 2017). These data represent a 50% increase in

prevalences compared to just 20 years ago (CDC, 2017). Obesity has grown across all spectrums of age, gender, and race. Since the 1960's, not only has obesity tripled among adult populations, it has also nearly quadrupled in children and adolescents, as demonstrated by CDC data (Fryar, et al, 2018 [1]; Fryar, et al, 2018 [2]):

Figure 4: CDC Data on Overweight, Obesity, and Severe Obesity in Adults in the U.S.

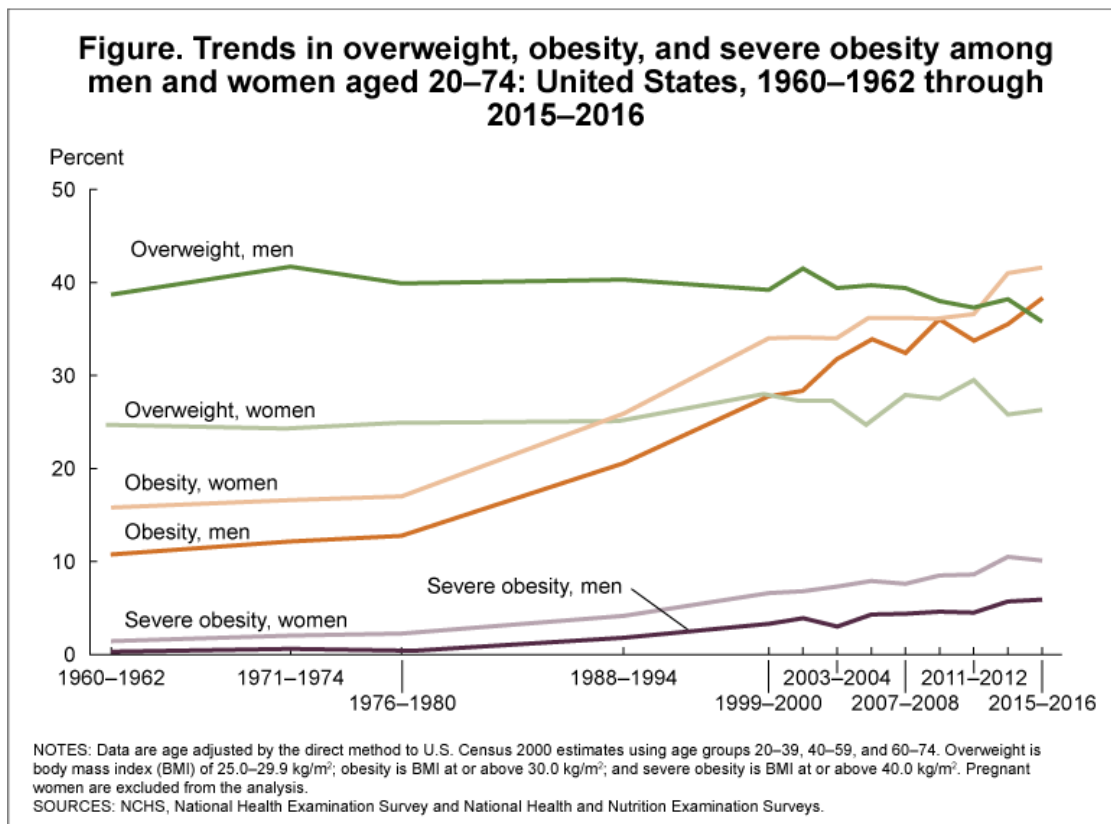
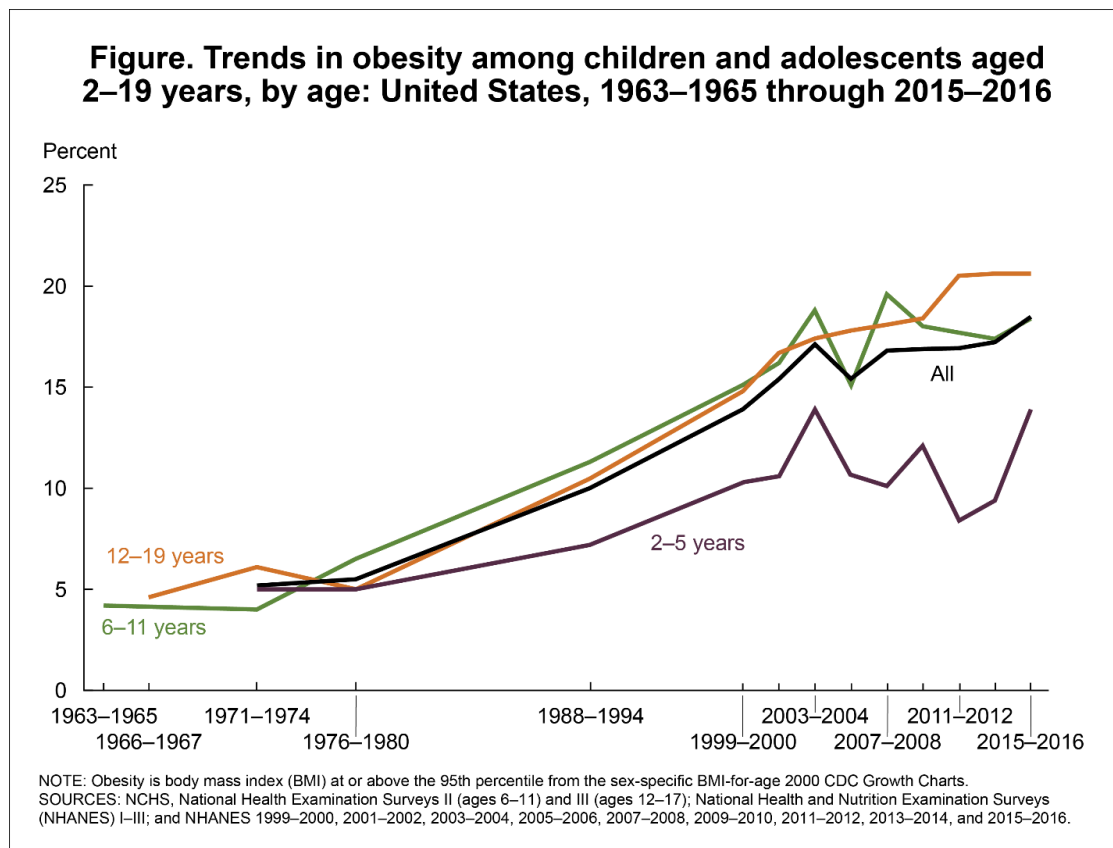


Figure 5: CDC Data on Overweight, Obesity, and Severe Obesity in Children and Adolescents in the U.S.



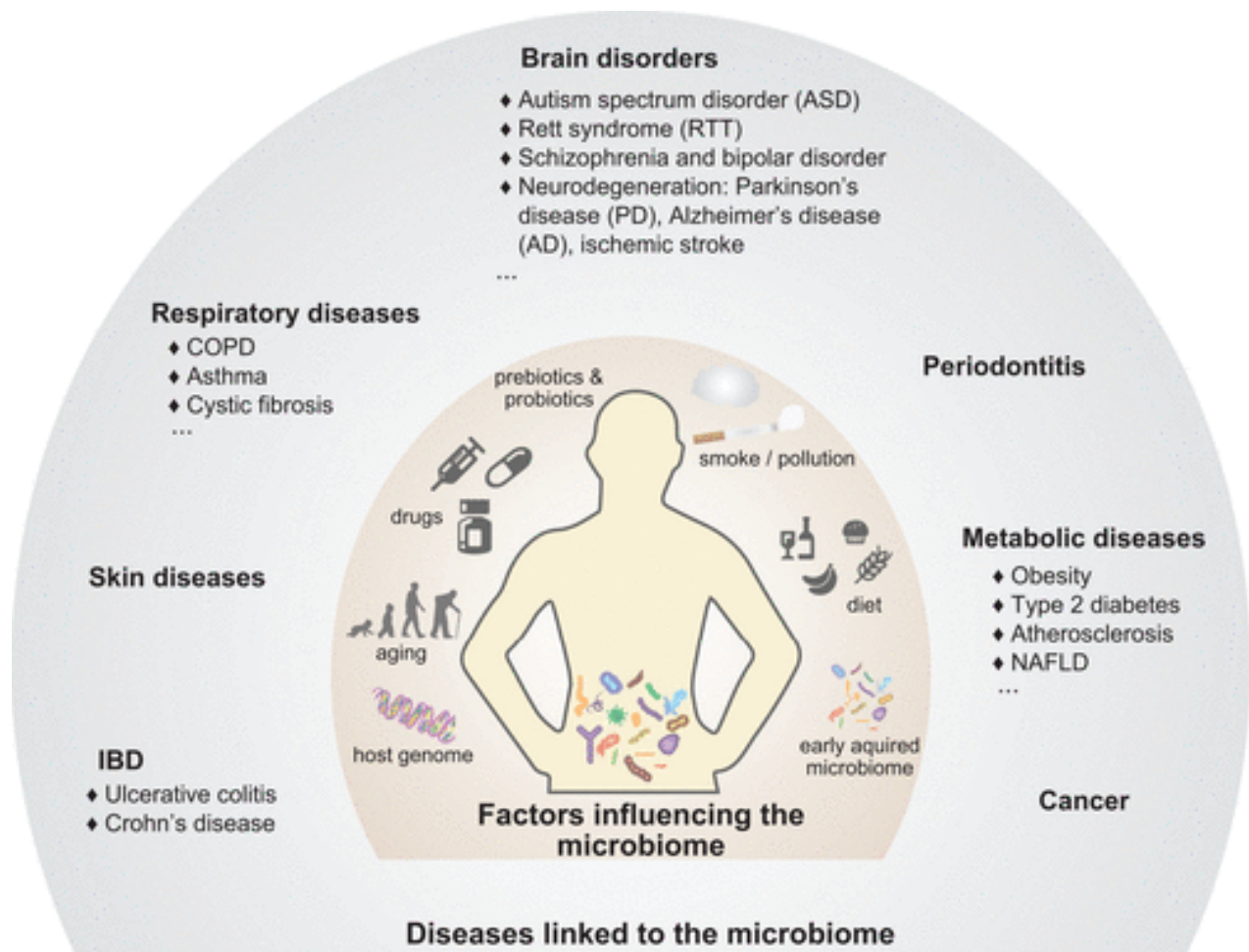
Obesity’s harmful health consequences are striking. It affects the body negatively in a wide variety of ways: it increases the risk of mortality, hypertension, hyperlipidemia, type 2 diabetes, coronary heart disease, stroke, gallbladder disease, osteoarthritis, sleep apnea, some cancers, lower quality of life, depression, anxiety, and difficulty with physical functioning (CDC, 2016). As is likely evident, this incurs a tremendous cost in terms of its economic impacts from direct and indirect costs. In 2008, the medical care costs of obesity in the United States was \$147 billion, and the annual nationwide productivity costs related to absenteeism secondary to obesity ranged from \$3.38 billion to \$6.38 billion (CDC, 2016). Obesity is therefore one of the most critically important health afflictions affecting the U.S. population today.

Obesity epidemics are not just limited to humans. There appears to be a concurrent plurality of obesity epidemics across species and across the same timeframe, which has raised questions for some researchers about the potential connections between the two. One study analyzing historic weight records for 24 animal populations that interact with humans (including domesticated animals, rodents, and primates) have shown this same pattern of weight gain over the past century that cannot be explained by statistical chance alone (Klimentidis, et al, 2011). The symmetry of selection phenomena is important when considering a common thread between convergent phenotypes, as they can emerge independently in different species. One critical selection modality is the human element, as anthropogenic influence is now a salient component of many selection phenomena (Thompson, 2013; Whitham, et al, 2006). As such, there are a variety of anthropogenic mechanisms through which animal obesity may be influencing human obesity. What accounts for this phenotype diffusion across species? One explanation is that this plurality of obesity across species may be reflective of a shared vulnerability such as constitutional or genetic changes within gut microbiomes.

The human gut microbiota consists of the trillions of symbiotic microorganisms harbored by an individual, including bacteria, viruses, eukaryotic microbes, and archaea (Shreiner, et al, 2016). The gut microbiome refers to the collective genomes within these microorganisms (Turnbaugh, et al, 2007). They contribute metabolic functions, inform our immune systems, and protect against other pathogens (Shreiner, et al, 2016). The hologenome is a construct which considers a host organism and all of its associated symbiotic microbiota (e.g. flora of the gut, skin, mouth, pulmonary tree, genitourinary tracts, etc.) as a single unit. The human genome is comprised of around 23,000 genes and a human microbiome encodes about 3,000,000 genes, which produce thousands of metabolites that replace important host functions (Falony, et al,

2016). A complex symbiosis between a human body and its microbiome exists, and if this interaction becomes disrupted, it can have detrimental, pathologic effects on both (Scotti, et al, 2017). Studies have demonstrated that dysbiosis (microbial imbalance) between humans and their gut microbiome can hold significant pathologic health impacts in terms of risk of obesity, certain diseases, and even mental health (Scotti, et al, 2017):

Figure 6: Diseases Linked to the Microbiome



In general, microbiota diversity is an approximate surrogate for the health of a microbiome, and lower diversity is considered a marker for dysbiosis (Valdes, 2018). However, we are finding that the presence or absence of certain key microbes may influence human metabolism and

health in specific ways. Further, the bacteria which comprise the gut microbiome have been shown to be transferrable not only from person-to-person but also zoonotically, lending credence to taking a One Health perspective regarding gut microbiota (Xiao, et al, 2016; Song, et al, 2013).

Over the past 150 years, humans have been artificially selecting many livestock for their metabolic phenotype (i.e. obesity), such as cattle and chickens (Bovine HapMap Consortium, et al, 2009; Zuidhof, et al, 2014). A chicken breed that was commercialized in 1957 and another breed from 2005 were recently raised under the same conditions with the same food, and the 2005 breed weighed four times more than the 1957 breed (Zuidhof, et al, 2014). By selecting for obesity in these livestock animals, we may have also been inadvertently selecting for gut microbiota that are obesogenic. Similar to plants and their relationship to soil, artificial selection of the gut microbiome can act on animals on short timescales (e.g. lifetimes), and is supported by experimental evidence in pigs, rats, and voles (Lyte, et al, 2016). We also have human twin and metagenomic data indicating that there are microbial genes associated with obesity and network-level differences in microbial metabolic genes between lean and obese persons (Greenblum, et al, 2012; Institute of Medicine (US) Food Forum, 2013; Turnbaugh, et al, 2009; Turnbaugh, et al, 2010). We have even discovered specific gut microbes that are associated with more obese or leaner individuals, e.g. *Christensenella* and *Akkermansia* (Beaumont, et al, 2016; Goodrich, et al, 2014; Ley, et al, 2006). In fact, there are animal experiments demonstrating that a fecal microbiota transplant from an obese animal to a lean animal will cause the lean animal to become obese (Backhed, et al, 2004). This phenomenon has caused researcher clinicians to begin trials on treating obesity with fecal microbiota transplants from lean individuals (Marotz & Zarrinpar, 2016).

Around 60% of human pathogens have zoonotic (mostly livestock) origins (Wardeh, et al, 2015). It is not a far reach to think that gut bacteria are similarly transferrable between animals and humans. In fact, there are studies confirming this idea and demonstrate that domesticated animals and humans share gut microbes with one another (Xiao, et al, 2016; Song, et al, 2013). We also have several mechanisms through which livestock gut microbiota can be transferred to humans. Raw cattle manure is frequently spread over fields harvested for human food. U.S. livestock animals alone produce 2 billion tons of manure per year, management of which is variably regulated state by state (Main, 2015). Many farms reuse animal feces as components of feed for their livestock as well. Cattle gut microbes are found in food consumed by humans (e.g. as seen in outbreaks of *Escherichia coli*). The classic One Health example follows: Cows may graze in a pasture next to a lettuce farm. Cattle may have guts populated by *E. coli* but remain asymptomatic. *E. coli* can be found present in their feces and their manure may contaminate the nearby lettuce field. Humans may then eat the contaminated lettuce and become infected with *E. coli* resulting in morbidity. A similar mechanism may be at play for obesogenic gut microbes. It is also possible that certain microbes are transmitted through milk as well (Funkhouser & Bordenstein, 2013). Further, veterinary antibiotic metabolites associated with adiposity have been found in the urine of Chinese school children (Wang, et al, 2016). County-level usage of veterinary antibiotics has also been demonstrated to overlay with county-level obesity in the U.S. (Riley, et al, 2013). Both of these examples further demonstrate potential transferrable pathways from livestock to humans in addition to other potential obesogens (i.e. substances that cause obesity). Finally, it is quite possible that horizontal gene transfer may be occurring between related animal and human gut bacteria, allowing for increased propensities for and susceptibilities to obesity.

Therefore, there may be hidden harms when a commercially favorable trait such as obesity is selected for in livestock. An individual's genome resides within a hologenome which in turn resides within the environmental metagenome (Theis, et al, 2016). Even without selecting for an individual's genome, the genetic milieu a person lives within (i.e. genetic and epigenetic effects) could be augmented by selection of the microbiome or environmental metagenome, and this selection could impact the individual's phenotype via transferable mechanisms. If a microbial extended phenotype were selected for artificially in an agricultural species which was then transferred to humans (e.g. obesity), then the extended phenotype in the human could be obscured partially by epistasis and pleiotropy (Voss, 2017).

C. Brief Ethical Analysis

We are ethically obligated to investigate and mitigate harms to human health, and the argument supporting this follows. We create obese livestock animals in order to satiate our meat consumption desires. This artificial selection for obese livestock animals may be creating obese humans indirectly. Obesity is currently an epidemic in the U.S. and is associated with an extensive list of serious and debilitating disease conditions. These diseases in turn would be of our own making, and disease is a harm. We have an ethical responsibility to appropriately address and curtail diseases that cause harm and suffering not only on an individual patient basis, but on public health and societal levels as well. Thus, we are ethically obligated to investigate the appropriateness of selecting livestock animals for obesity as it relates to human health.

This newfound information around the human hologenome and how it interacts with livestock animals and the environmental metagenome add another piece of ethical complexity to the context. A *prima facie* ethical argument in environmental and food ethics states that we should all decrease our meat consumption because it benefits human health, the environment,

and animal welfare (Pickles, 2017). It helps humans (bioethics) by improving human health through decreasing cardiovascular disease, colorectal cancer, obesity, and other health maladies associated with meat consumption. It helps the environment (environmental ethics) by reducing harmful climate change through decreasing deforestation, reducing methane production, freeing land for conservation, decreasing resources required for livestock, etc. It helps animals (animal ethics) by reducing cruel living conditions, decreasing slaughtering, freeing area for conservation of wild animals, etc.

The benefits of decreased meat consumption at a societal level are ethically obvious and inarguable. However, suppose humans were more inclined to continue their current meat consumption habits. It is not a difficult leap to assume that those who advocate for significantly decreasing our meat consumption face an incredible amount of inertia. This section will therefore examine the ethics of meat production and consumption in the context of the hologenome interaction and on the assumption that human behavior regarding meat consumption will not change in a meaningful way. Another critical consideration in ethically analyzing this situation is that the world is currently experiencing a looming global catastrophe manifested by climate change, and livestock animals contribute significantly to that in a detrimental fashion. In fact, livestock animals and global meat production has continued to increase rapidly over the past 50 years, as total production has grown 4-5-fold since 1961, as demonstrated below (Ritchie & Roser, 2017):

Figure 7: Global Livestock Counts

Global livestock numbers over the long-term

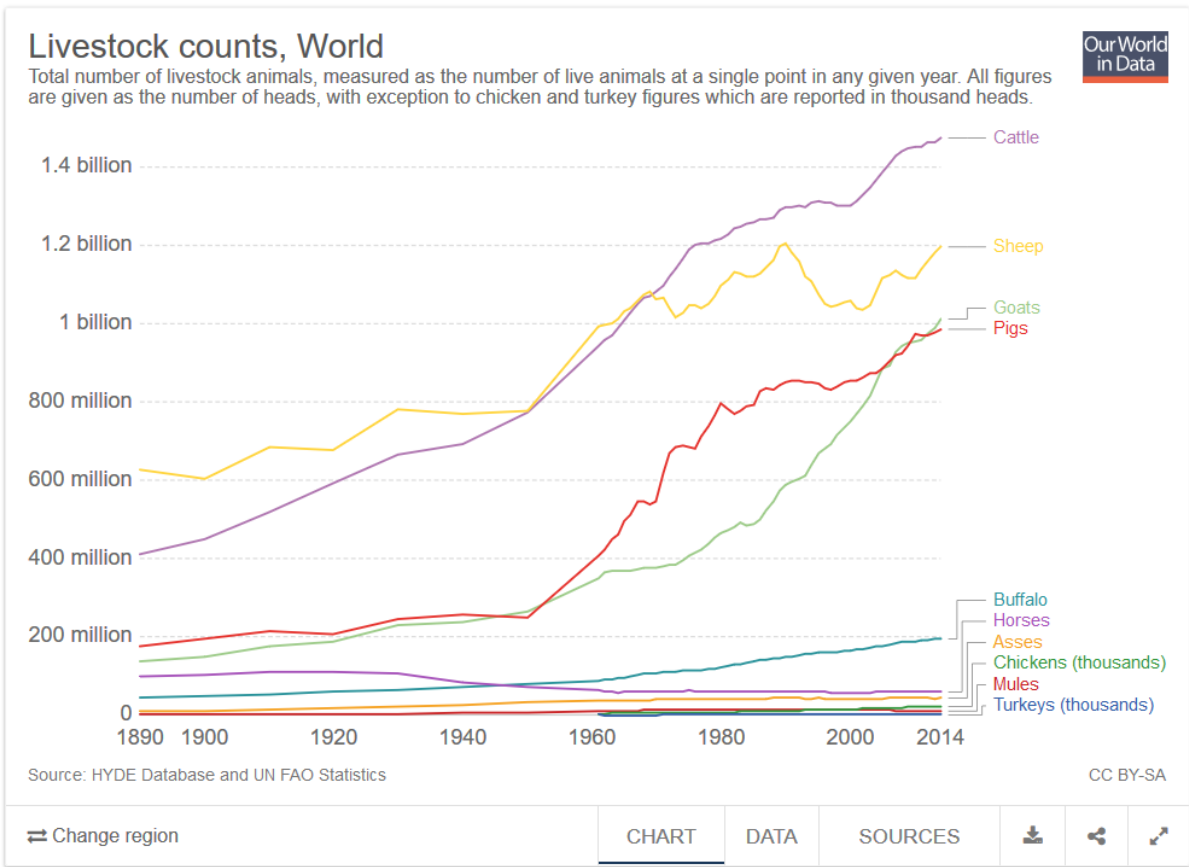
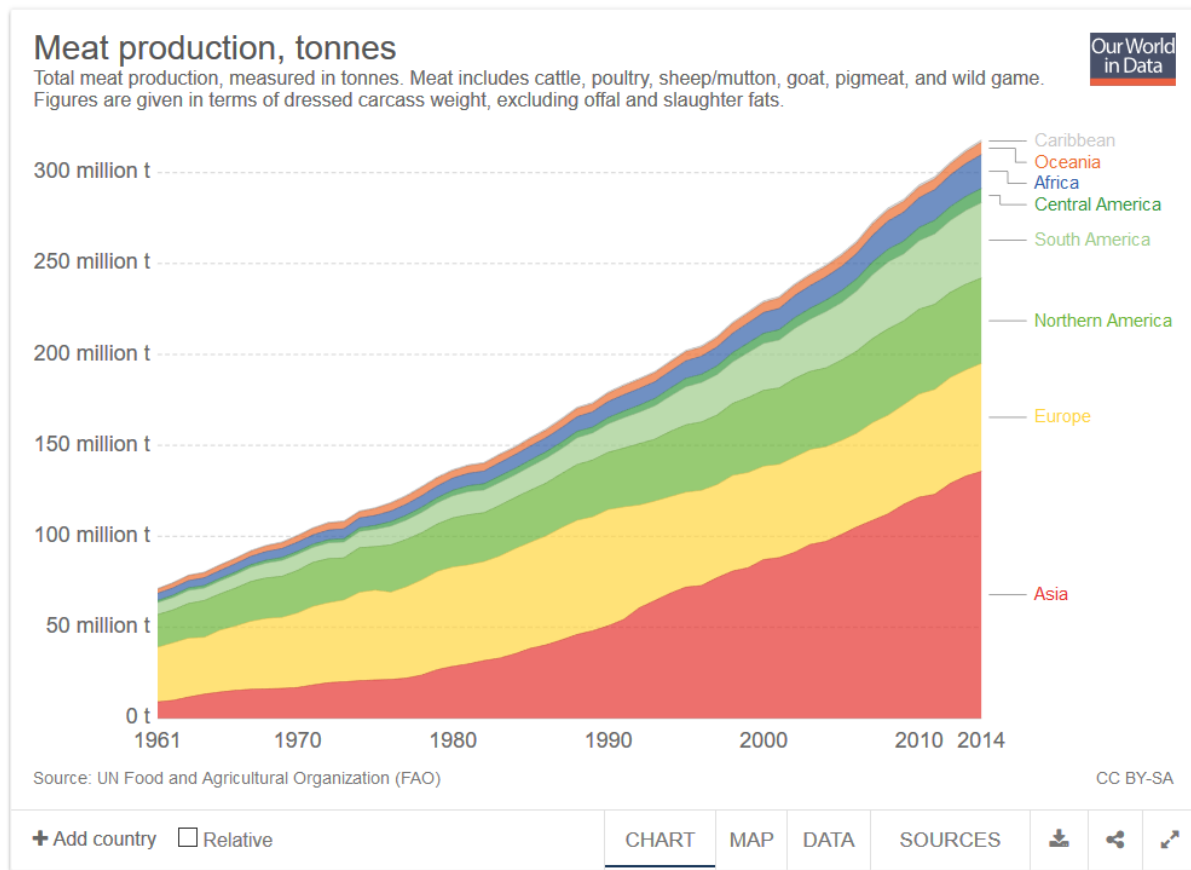
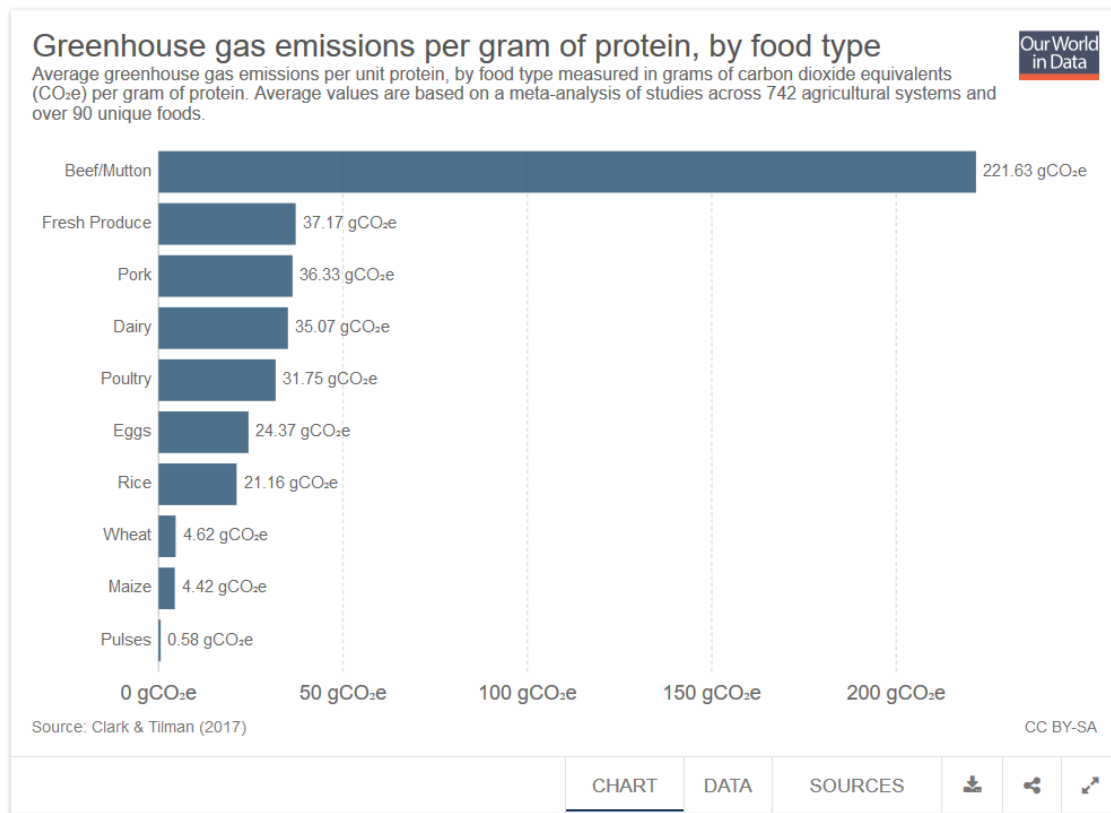


Figure 8: Global Meat Production



Furthermore, the meat produced for consumption by livestock animals leaves a significantly higher greenhouse gas footprint when compared to vegetable-based food options, as shown below (Ritchie & Roser, 2017):

Figure 9: Greenhouse Gas Emissions by Food Type



By creating more metabolically efficient obese livestock animals, one creates animals that are less harmful to the environment and climate change. We can decrease livestock impacts on climate change by selecting for animals that grow faster and grow larger. The less time to large size, the less time there is a strain on the environment. The greater the efficiency ratio of input to output, the fewer resources and animals needed for output. Rather than having to feed and care for 4 chickens, one can instead raise 1 with the same meat output. This obesity selection approach requires less land and resource input as well as limits greenhouse gas emissions compared to a lean animal approach, assuming meat consumption rates remain the same (which the data suggests is the case). Therefore, the ethical dilemma is that obese animals appear to be a partial solution to feeding the meat demands of the world with climate change-limiting effects,

yet the process in itself may be creating obese humans prone to serious diseases. We are trading one public health issue for another.

V. Application of the Evidence Appraisal & Actionability Tool

It is therefore evident that the hologenome-livestock-obesity problem is one that holds potentially significant ethical implications. Further, it vividly illustrates a case of radical uncertainty, yet we must nevertheless decide how we ought to respond when presented with such evidence. To demonstrate the utility of the Evidence Appraisal & Actionability Tool, we can apply it to this scenario. First, in assessing the strength of evidence of the problem, there are several key knowledge gaps which would require investigation as to whether the proposed association is in fact robust. One gap is the demonstration of the transmission of livestock gut microbiota to human populations. Though we have tangential evidence of such, as discussed through various metabolite surveys and ecologic-level data, there must be more vigorous data to confirm this transmission pathway. Another gap is identifying a more robust catalog of obesogenic microbes in livestock as well as in humans, and to then confirm if these same microbes are capable of zoonotic and/or reverse-zoonotic transmission. It would also be worthwhile to demonstrate if horizontal gene transfer between zoonotic gut microbiota would be possible and to document whether obesogenic genes were subjected to this transfer. One must also consider information regarding the epigenetic interactions between a host's genome and their microbiome to see if obesogenic microbes selectively impact some individuals or populations more than others. Much more substantial research must be conducted to confirm the hypothetical biologic and transmission mechanisms offered in this proposed scenario, as much of

them are based upon related or tangential mechanisms but little direct evidence. Thus, the strength of evidence is weak.

The second step is to determine the magnitude of impact of the hologenome-livestock-obesity interaction. Given the discussion above, the potential impacts in responding to this are substantial. We also have extensive data regarding human obesity and its detrimental health effects. However, we are still lacking in knowing just how extensively the gut microbiome impacts human obesity. It would be necessary to conduct further studies regarding specific gut microbiota species and their obesogenic potential. It would also require an estimation of obesogenic gut microbiota on human obesity itself in terms of risk. In addition, one would need to know the number of people such gut microbiota would impact, which would necessitate host gene-gut microbe gene interaction prevalence and details regarding exposure (e.g. geography, intensity, dose-response, population sizes). Without more precise estimates regarding the individual-level impact of gut microbiota on obesity and the populations affected, it is difficult to accurately assess how impactful it is. However, given that obesity is so widespread and causes significant morbidity and mortality, even a small decrease would yield very meaningful results. Therefore, the magnitude of impact at this stage is substantial. However, with more information it could become moderate or weak.

Since at this point the strength of evidence is weak and the magnitude of impact is substantial, the recommendation grade is C1. We therefore have a strong impetus for conducting more research in the area. However, it is still much too early to seriously consider it in discussions about obesity prevention and control in humans. This scenario clearly illustrates a case of radical uncertainty with potentially huge impacts. It demonstrates how the Evidence Appraisal & Actionability Tool can help us decide what level of certainty we are at regarding the

information presented to us, recommend obligations as to how we ought to treat such data in our decision-making, and even lead us to what our next steps should be. Further refinement of the tool might also offer guidance regarding questions such as: if some of the uncertain connections are proven what interim next steps might take place; what might it take to move from C1 to B; what does the move between grades in terms of research; what action steps might need to take place; and what ethical issues or dilemmas might arise related to the next actions steps?

VI. Conclusions

The Evidence Appraisal & Actionability Tool itself is a tool of epistemology and consequence – it concerns the appraisal of knowledge with varying degrees of certainty in addition to potential impacts and actions. Further, it is designed to help an individual or group evaluate what kind of situation of uncertainty they are facing. The grading is intended to take this one step further to make credence actionable and determine what a person's ethical responsibility is in light of that. Its ethical relevance is derived from an individual or group utilizing the grade in some context as a recommendation for how they ought to act when confronted by varying degrees of uncertainty, and particularly in cases of radical uncertainty. It offers a framework for approaching an ethically responsible deliberative process which may allow for more ethical outcomes based upon those judgments.

One implication of this tool is the resultant ethical impetus for conducting high quality research in order to better inform our decisions. Through this ethical analysis and construction of a decision-making framework, we reveal something interesting about how research relates to bioethics and responsible decision-making. This approach comes from a different perspective

than “if we learn new treatment modalities or harmful exposures to avoid, we can benefit more people” – instead, it generates an ethical impetus from research’s influence on the certainty of our reasons for making decisions with ethical implications.

A decision that impacts health without sufficient data to inform the reasoning behind that decision is reckless and can therefore be unethical. However, we must sometimes make decisions with what data we have, even if it is suboptimal in validity, reliability, and generalizability. A decision made with greater confidence linking action with intended consequence is more ethical than one in which there is a great gamble and uncertainty related to the action and its consequences. A decision may produce unintended harmful effects, negligible effects, or beneficial effects. Quality research can provide us with greater confidence in our decision-making. Therefore, there is an ethical impetus to conduct quality research in order to better inform our decision-making such that we choose the best, most ethical course of action.

Future development of the Evidence Appraisal & Actionability Tool might include the construction of an ethical checklist such that the tool would become a component of a larger toolkit. This ethical checklist could offer aid to guide the deliberation regarding evidence appraisal and actionability to more explicitly incorporate discussion of ethical considerations in making decisions about what action to take.

Humans seemingly have an innate drive for knowledge and understanding. We should embrace our inquisitive nature in a meaningful way so that we can be more assured in our action-consequence flow to improve our ethical decision-making. By removing risk, we create a more ethically conducive decision-making environment. Yet even within the suboptimal environment of radical uncertainty, there is an ethical way to approach and weigh such information – the Evidence Appraisal & Actionability Tool offers aid in this epistemologic endeavor.

Works Cited

1. ACCF/AHA Task Force on Practice Guidelines. (2010). Methodology manual and policies from the ACCF/AHA task force on practice guidelines. *American College of Cardiology Foundation and American Heart Association*.
<http://assets.cardiosource.com/Methodology_Manual_for_ACC_AHA_Writing_Committees.pdf and http://my.americanheart.org/idc/groups/ahamah-public/@wcm/sop/documents/downloadable/ucm_319826.pdf>.
2. Backhed F, Ding H, Wang T, Hooper LV, Koh GY, Nagy A, Semenkovich CF, and Gordon JI. (2004). The gut microbiota as an environmental factor that regulates fat storage. *Proc Natl Acad Sci USA*. 101: 15718–15723.
3. Beaumont M, Goodrich JK, Jackson MA, Yet I, Davenport ER, Vieira-Silvas S, Debelius J, Pallister T, Mangino M, Raes J, Knight R, Clark AG, Ley RE, Spector TD, and Bell JT. (2016). Heritable components of the human fecal microbiome are associated with visceral fat. *Genome Biol*. 17(1): 189.
4. Bovine HapMap Consortium, Gibbs, RA, Taylor, JF, Van Tassell, CP, Barendse, W, Eversole, KA...Dodds, KG. (2009). Genome-wide survey of SNP variation uncovers the genetic structure of cattle breeds. *Science*. 324(5926): 528-532.
5. CDC. (2016). “Overweight and Obesity.” *Centers for Disease Control and Prevention*. <<https://www.cdc.gov/obesity/adult/defining.html>>.
6. CDC. (2017). “Obesity and Overweight.” *National Center for Health Statistics*. Centers for Disease Control and Prevention. <<https://www.cdc.gov/nchs/fastats/obesity-overweight.htm>>.
7. Dhurandhar, EJ and SW Keith. (2014). The aetiology of obesity beyond eating more and exercising less. *Best Practice & Research Clinical Gastroenterology*. 28: 533-544.
8. Faloney, G, M Joossens, S Vieira-Silva, J Wang, Y Darzi, K Faust, A Kurilshikov, MJ Bonder, M Valles-Colomer, D Vandeputte, RY Tito, S Chaffron, L Rymenans, C Verspecht, L De Sutter, G Lima-Mendez, K D’hoel, K Johnckheere, D Homola, R Garcia, EF Tigchelaar, L Eeckhaedt, J Fu, L Henckaerts, A Zhernakova, C Wijmenga, and J Raes. (2016). Population-level analysis of gut microbiome variation. *Science*. 352(6285): 560-564.
9. Fryar, CD, Carroll, MD, and Ogden CL. (2018). Prevalence of overweight, obesity, and severe obesity among adults aged 20 and over: United States, 1960-1962 through 2015-2016. *National Center for Health Statistics*. Centers for Disease Control and Prevention. <https://www.cdc.gov/nchs/data/hestat/obesity_adult_15_16/obesity_adult_15_16.htm>.
10. Fryar, CD, Carroll, MD, and Ogden CL. (2018). Prevalence of overweight, obesity, and severe obesity among children and adolescents aged 2-19 years: United States, 1963-1965 through 2015-2016. *National Center for Health Statistics*. Centers for Disease Control and Prevention. https://www.cdc.gov/nchs/data/hestat/obesity_child_15_16/obesity_child_15_16.htm
11. Funkhouser, LJ and SR Bordenstein. (2013). Mom knows best: the universality of maternal microbial transmission. *PLoS Biology*. 11(8): e1001631.

12. Goodrich JK, Waters JL, Poole AC, Sutter JL, Koren O, Blekhman R, Beaumont M, Van Treuren W, Knight R, Bell JT, Spector TD, Clark AG, and Ley RE. (2014). Human genetics shape the gut microbiome. *Cell*. 159(4): 789-99.
13. Greenblum S, Turnbaugh PJ, and Borenstein E. (2012). Metagenomic systems biology of the human gut microbiome reveals topological shifts associated with obesity and inflammatory bowel disease. *PNAS*. 109(2):594–599.
14. Halperin, JL, GN Levine, SM Al-Khatib, KK Birtcher, B Bozkurt, RG Brindis, JE Cigarroa, LH Curtis, LA Fleisher, F Gentile, S Gidding, MA Hlatky, J Ikonmidis, J Joglar, SJ Pressler, and DN Wijesundera. (2015). Further evolution of the ACC/AHA clinical practice guideline recommendation classification system: A report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines. *Circulation*. 133: 1426-1428.
15. Hill, AB. (1965). “The Environment and Disease: Association or Causation?” *Proceedings of the Royal Society of Medicine*. 58(5): 295–300.
16. Hume, D. (1779). “An enquiry concerning human understanding.” In D. Hume, *Essays and treatises on several subjects, Vol. 2. Containing An enquiry concerning human understanding, A dissertation on the passions, An enquiry concerning the principles of morals, and The natural history of religion*. 3-212.
17. Institute of Medicine (US) Food Forum. (2013) The Human Microbiome, Diet, and Health: Workshop Summary. Washington (DC): National Academies Press (US). 4, Influence of the Microbiome on the Metabolism of Diet and Dietary Components.
<https://www.ncbi.nlm.nih.gov/books/NBK154098/>
18. Klimentidis, YC, Beasley, TM, Lin, HY, Murati, G, Glass, GE, Guyton, M...Allison, DB. (2011). Canaries in the coal mine: a cross-species analysis of the plurality of obesity epidemics. *Proceedings of the Royal Society of London B: Biological Sciences*. 278(1712): 1626-1632.
19. Ley RE, Turnbaugh PJ, Klein S, and Gordon JL. (2006). Microbial ecology: human gut microbes associated with obesity. *Nature*. 444: 1022–1023.
20. Lyte, M, Fodor, AA, Chapman, CD, Martin, GG, Perez-Chanona, E, Jobin, C, and Dess, NK. (2016). Gut microbiota and a selectively bred taste phenotype: a novel model of microbiome-behavior relationships. *Psychosomatic Medicine*. 78: 610-619.
21. Main, D. (2015). Two numbers: animal manure a growing headache in America. *Newsweek Magazine*. <<https://www.newsweek.com/2015/12/18/two-numbers-animal-manure-growing-headache-america-402205.html>>.
22. Marotz, CA and A Zarrinpar. (2016). Treating obesity and metabolic syndrome with fecal microbiota transplantation. *Yale J Biol Med*. 89(3): 383-388.
23. Morris, WE and Brown, Charlotte R. (2017). “David Hume.” *The Stanford Encyclopedia of Philosophy*. Zalta, EN (ed.). <<https://plato.stanford.edu/archives/spr2017/entries/hume/>>.

24. Pickles, M. (2017). “The ethical arguments against eating meat.” *University of Oxford*. <<http://www.ox.ac.uk/news/arts-blog/ethical-arguments-against-eating-meat>>.
25. Riley, LW, Raphael, E, and Faerstein, E. (2013). Obesity in the United States – dysbiosis from exposure to low-dose antibiotics? *Frontiers in Public Health*. 1: 69.
26. Ritchie, H and M Roser. (2017). Meat and seafood production and consumption. *Our World in Data*. <<https://ourworldindata.org/meat-and-seafood-production-consumption#how-are-land-use-requirements-and-greenhouse-gas-emissions-calculated-for-food-products>>.
27. Schick, A. (2016). Whereto speculative bioethics? Technological visions and future simulations in a science fictional culture. *Medical humanities*. 42(4):225-231.
28. Scotti, E., Boué, S., Sasso, G. L., Zanetti, F., Belcastro, V., Poussin, C., ... Hoeng, J. (2017). Exploring the microbiome in health and disease: Implications for toxicology. *Toxicology Research and Application*. <<https://doi.org/10.1177/2397847317741884>>.
29. Shreiner, AB, JY Kao, and VB Young. (2016). The gut microbiome in health and in disease. *Curr Opin Gastroenterol*. 31(1): 69-75.
30. Song, SJ, Lauber, C, Costello, EK, Lozupone, CA, Humphrey, G, Berg-Lyons, D...Knight, R. (2013). Cohabiting family members share microbiota with one another and with their dogs. *Elife*. 2: e00458.
31. Theis, KR, Dheilly, NM, Klassen, JL, Brucker, RM, Baines, JF, Bosch, TC...Bordenstein, SR. (2016). Getting the hologenome concept right: an eco-evolutionary framework for hosts and their microbiomes. *mSystems*. 1(2): e00028-16.
32. Thompson, JN. (2013). *Relentless evolution*. Chicago, IL: University of Chicago Press.
33. Turnbaugh PJ, Ley RE, Hamady M, Fraser-Liggett CM, Knight R, and Gordon JI. (2007). The human microbiome project. *Nature*. 449:804–810.
34. Turnbaugh PJ, Hamady M, Yatsunenko T, Cantarel BL, Duncan A, Ley RE, Sogin ML, Jones WJ, Roe BA, Affourtit JP, Egholm M, Henrissat B, Heath AC, Knight R, and Gordon JI. (2009). A core gut microbiome in obese and lean twins. *Nature*. 457(7228):480–484.
35. Turnbaugh PJ, Quince C, Faith JJ, McHardy AC, Yatsunenko T, Niazi F, Affourtit J, Egholm M, Henrissat B, Knight R, and Gordon JI. (2010). Organismal, genetic, and transcriptional variation in the deeply sequenced gut microbiomes of identical twins. *PNAS*. 107(16):7503–7508.
36. USPSTF. (2018). “Grade Definitions.” *USPSTF*. <<https://www.uspreventiveservicestaskforce.org/Page/Name/grade-definitions>>.
37. USPSTF. (2017). “Final Update Summary: Folic Acid for the Prevention of Neural Tube Defects: Preventive Medication.” *USPSTF*. <<https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/folic-acid-for-the-prevention-of-neural-tube-defects-preventive-medication>>.

38. Valdes, AM, J Walter, E Segal, and TD Spector. (2018). Role of the gut microbiota in nutrition and health. *BMJ*. 361: k2179.
39. Voss, JD, MS Goodson, and JC Leon. (2017). Phenotype diffusion and one health: a proposed framework for investigating the plurality of obesity epidemics across many species. *Zoonoses Public Health*. 65: 279-290.
40. Wang, H, Wang, N, Wang, B, Fang, H, Fu, C, Tang, C...Jiang, Q. (2016). Antibiotics detected in urines and adipogenesis in school children. *Environment International*. 89: 204-211.
41. Wardeh, M, Risley, C, McIntyre, MK, Setzkorn, C, and Baylis, M. (2013). Database of host-pathogen and related species interactions, and their global distribution. *Scientific Data*. 2: 150049.
42. Whitham, TG, Bailey, JK, Schweitzer, JA, Shuster, SM, Bangert, RK, LeRoy, CJ...Wooley, SC. (2006). A framework for community and ecosystem genetics: from genes to ecosystems. *Nature Reviews Genetics*. 7: 510-523.
43. Xiao, L, Estelle, J, Kiilerich, P, Ramayo-Caldas, Y, Xia, Z, Feng, Q...Wang, J. (2016). A reference gene catalogue of the pig gut microbiome. *Nature Microbiology*. 16161.
44. Zuidhof, MJ, Schneider BL, Carney VL, Korver DR, and Robinson FE. (2014). Growth, efficiency, and yield of commercial broilers from 1957, 1978, and 2005. *Poult Sci*. 93(12): 2970-82.

Hunter Jackson Smith

hunterjsmith11@gmail.com

January 7th, 1991

+1-239-823-8353

EDUCATION

- **Johns Hopkins Bloomberg School of Public Health** Jan 2017 – May 2019
 - *Master of Bioethics*
 - GPA: 4.00
- **Tulane University School of Medicine** Jun 2013 – May 2017
 - *Doctor of Medicine*
 - 4-year MD/MPH combined degree program
 - Internship in Egypt at WHO Eastern Mediterranean Region Headquarters (2017 - 3 months)
- **Tulane University School of Public Health and Tropical Medicine** Jun 2013 – May 2017
 - *Master of Public Health*
 - Major: Epidemiology
 - GPA: 3.88
- **Tulane University** Aug 2009 – May 2013
 - *Bachelor of Arts with honors*
 - Majors: Philosophy, Religious Studies
 - Minors: Public Health, Latin American Studies
 - GPA: 3.87, *summa cum laude*
 - Study abroad in South Africa at University of Cape Town (2012 - 6 months)
 - Study abroad in China at Fudan University (2012 - 2 months)

POSTGRADUATE MEDICAL TRAINING

- **General Preventive Medicine Residency** Jul 2018 – Jul 2020
 - National Capital Consortium (Uniformed Services University and Walter Reed Medical Center)
 - First-ever Army resident selected for the program
- **Certificate in General Preventive Medicine** Jul 2018 – May 2019
 - Uniformed Services University (Bethesda, MD)

- **Certificate in Global Health** Oct 2018 – May 2019
 - Johns Hopkins Bloomberg School of Public Health (Baltimore, MD)
- **Certificate in Clinical Tropical Medicine and Travelers' Health** Feb 2019 – May 2019
 - Uniformed Services University (Bethesda, MD)
 - American Society of Tropical Medicine and Hygiene (ASTMH) Diploma Course
- **Transitional Preliminary Internship** Jun 2017 – Jun 2018
 - Tripler Army Medical Center (Honolulu, HI)

HONORS & AWARDS

- | | |
|---|------------|
| ● Delta Omega Public Health Honor Society | 2019 |
| ● U.S. Public Health Service Excellence in Public Health Award | 2017 |
| ● MD/MPH Student Award for Excellence | 2017 |
| ● Prim Smith Ethics Award | 2017 |
| ● B. Bernard Weinstein Award | 2015, 2017 |
| ○ 'Most outstanding original research on the history of medicine' | |
| ● Isaac Ivan Lemann Award | 2014, 2016 |
| ○ 'Most outstanding paper on the ethical aspects of medicine' | |
| ● U.S. Army Certificate of Achievement | 2014 |
| ○ 'For exceptional leadership and selfless service' | |
| ● MD/MPH Combined Degree Merit-Based Scholarship Award | 2013 |
| ● Phi Beta Kappa Honor Society | 2013 |
| ● Senior Honors Scholar in Philosophy | 2013 |
| ○ Top student in Philosophy Department | |
| ● Senior Honors Scholar in Religious Studies | 2013 |
| ○ Top student in Religious Studies Department | |

- **Creative Scholars Program** 2011
 - Early acceptance to Tulane University School of Medicine

LEADERSHIP & ACTIVITIES

- **Captain in the U.S. Army Medical Corps** Jan 2013 – Present
 - Health Professions Scholarship Program (2013-2017)
- **Postdoctoral Researcher at the Johns Hopkins BRIDGES Center** Dec 2018 – Present
 - The Center for Bridging Infectious Disease, Genomics, and Society (BRIDGES) is an NIH-designated Center of Excellence in ELSI (Ethical, Legal, and Social Implications) Research.
 - Awarded a \$30,000 scholarship for selection into the program.
- **Member of the Walter Reed Medical Center Ethics Committee** Jul 2018 – Present
 - The committee provides ethics-related education, consultation, and policy review for WRNMMC.
- **Subject Matter Expert for the DoD Medical Ethics Center** Jan 2019 – Present
 - Contributing and collaborating with the DMEC to create medical ethics content for the DoD military health system which reaches all Army, Navy, and Air Force providers.
- **Theme Issue Editor for the *AMA Journal of Ethics*** Nov 2018 – Aug 2020
 - Currently overseeing the development of the August 2020 issue of the *AMA Journal of Ethics* entitled “Ethics in Managing Pain During an Opioid Epidemic.”
 - Responsible for creating the journal edition’s theme, soliciting scholarly contributions, promoting the issue through relevant media, and writing commentary on the subject.
- **General Preventive Medicine Program House Staff Council Representative**
 - Elected by peers to represent the USU General Preventive Medicine program to the WRNMMC Resident Council. Jul 2018 – Jul 2019
- **Resident Liaison to the ACPM Resident Physician Section** Nov 2018 – Jun 2019
 - Selected to represent the USU General Preventive Medicine program to the ACPM’s national Resident Physician Section.

- **Teaching Assistant for Johns Hopkins Bloomberg School of Public Health**
 - TA for the graduate course “Germs, Genes, Patients, and Populations.” Responsible for grading coursework, delivering lectures, facilitating group discussions, and organizing guest speakers. Mar 2019 – May 2019

- **Member of Tripler Army Medical Center Ethics Committee** Jun 2017 – Jun 2018
 - Assisted in resolving complicated ethical problems involving issues that affect the care and treatment of patients. Called upon for urgent ethics consults and attended formal monthly meetings to discuss previous consults and hospital policies. Educated departments on ethics consults and topics.

- **Transitional Year Program Representative to the Resident Council** Jun 2017 – Jun 2018
 - Elected by peers to represent the interests and concerns of the Transitional Year program to the Tripler Army Medical Center Resident Council.

- **Member of Tulane Medical Center Ethics Committee** Aug 2013 – May 2017
 - Assisted in resolving complicated ethical problems involving issues that affect the care and treatment of patients. Called upon for urgent ethics consults and attended formal monthly meetings to discuss previous consults and hospital policies.

- **Medical Ethics Education Curriculum Developer** Jun 2014 – May 2017
 - Developed and implemented a novel medical ethics lesson framework for first- and second-year medical students. The pilot module was successful and retained in perpetuity for future classes.
 - Worked with administration and course directors to further improve the medical ethics curriculum and expanded the pilot framework to additional modules.

- **National Board Member of the AMA Committee on Bioethics and Humanities**
 - The committee is responsible for facilitating student discussion on topics in medical ethics, advocating for the importance of medical ethics, creating AMA bioethics programming, and promoting the online version of the AMA's monthly bioethics journal, *AMA Journal of Ethics*. Aug 2016 – May 2017

- **National Board Member of the ACPM Medical Student Section** Aug 2016 – May 2017
 - The ACPM MSS leadership is responsible for overseeing MSS activities, providing support for the creation of local interest groups, and generating awareness and enthusiasm for

Preventive Medicine.

- **WHO Eastern Mediterranean Region Internship** Nov 2016 – Feb 2017
 - Intern for the World Health Organization at the regional headquarters in Cairo, Egypt. Assigned to the Division of Noncommunicable Diseases and Mental Health surveillance unit.
 - Duty work included leading a Middle East NCD research prioritization project, aiding in the publication of the *Eastern Mediterranean Health Journal*, and working on current WHO NCD research.
- **Clinic Coordinator for Bethel Colony South** Sep 2013 – May 2015
 - Expanded variety of programs from exclusively tuberculosis screening and influenza vaccination to further include HIV testing and counseling, physician examinations, and Hepatitis C screening.
 - Responsible for supervising medical student volunteers, organizing the clinic for tuberculosis skin testing and influenza vaccination, and administering relevant medical care.
- **President of Tulane Bioethics Interest Group** Dec 2013 – May 2015
 - Tripled attendance from previous year, increased budget by 250%, and held monthly meetings.
 - Responsible for selecting topics and articles for discussion, organizing student attendance, and leading and moderating the group meetings.

RESEARCH EXPERIENCE

- **Uniformed Services University Epidemiology Research** Sep 2018 – Present
 - *An Umbrella Review of Systematic Probiotic Meta-Analyses with Subgroups or Meta-Regression*
- **Johns Hopkins Bioethics Research** Dec 2018 – Present
 - *The Ethics of Shared Decision-Making in Terminally Ill Adolescent Populations*
 - Manuscript:
Smith, HJ, Kelly-Hedrick, M, Docchio, C, & Altiery De Jesus, V. “The Ethics of Shared Decision-Making in Terminally Ill Adolescent Populations.” Pending submission.
- **Johns Hopkins Bioethics Master’s Thesis** Jan 2019 – Present
 - *Ethical Decision-Making Under Radical Uncertainty*

- Manuscript:
Smith, HJ. “Ethical Decision-Making Under Radical Uncertainty.” Pending submission.

- **Johns Hopkins Bioethics Research** Sep 2018 – Apr 2019
 - *An Ethical Investigation into the Hologenome: The Intersection of Agriculture, Genetics, and the Obesity Epidemic*
 - Poster Presentation:
Smith, HJ. (April 2019). *An Ethical Investigation into the Hologenome: The Intersection of Agriculture, Genetics, and the Obesity Epidemic*. Poster Presented at: NHGRI Annual Conference; St. Louis, MO.

- **Tripler Army Medical Center Quality Improvement Research** Jul 2017 – Jun 2018
 - *An Evaluation of Multidrug-Resistant Organism Isolation Precaution Policy and Clearance Protocols*
 - Poster Presentation:
Smith, HJ & Kloetzel, MK. (May 2018). *An Evaluation of Multidrug-Resistant Organism Isolation Precaution Policy and Clearance Protocols*. Poster Presented at: Donald J Person Poster Symposium; Honolulu, HI.

- **World Health Organization Research** Nov 2016 – Nov 2017
 - *An Overview and Analysis of Noncommunicable Disease Research Priorities in the Eastern Mediterranean Region*
 - Poster Presentation:
Kobeissi, L, **Smith, HJ**, & Alwan A. (November 2017). *An Overview and Analysis of Cardiovascular Disease Research Priorities in the Eastern Mediterranean Region*. Poster presented at: American Public Health Association Annual Meeting and Exposition; Atlanta, GA.

- **Tulane DeBakey Scholars Program** Aug 2013 – May 2017
 - *The Divergence of Personal Freedom and the Public Health Good*
 - The DeBakey Scholars Program is aimed at fostering self-directed, life-long learning by allowing select students to perform a 4-year longitudinal research project.
 - Poster Presentation:
Smith, HJ. (February 2017). *The Divergence of Personal Freedom and the Public Health Good*. Poster presented at: Tulane Health Sciences Research Symposium; New Orleans, LA.

- **Tulane Epidemiology Master’s Thesis** Jun 2015 – Apr 2017
 - *An Ethical and Epidemiologic Analysis of U.S. Army Tobacco Health Policy*
 - Manuscript:
Smith, HJ and TN Rieder. “The ethical obligations of a military to the health of its members: An analysis of U.S. military tobacco policy.” Pending submission.

- Poster Presentation:
Smith, HJ. (March 2017). *An Ethical and Epidemiologic Analysis of U.S. Army Tobacco Health Policy*. Poster presented at: Tulane Delta Omega Society Poster Symposium; New Orleans, LA.

- **Tulane Bioethics Research** Jan 2013 – Mar 2016
 - *The Ethical Implications and Religious Significance of Organ Transplantation Payment Systems*
 - Peer-Reviewed Publication:
Smith, HJ. (2016). “The ethical implications and religious significance of organ transplantation payment systems.” *Medicine, Health Care, and Philosophy*. 19(1): 33-44. PMID: 25772853.
 - Poster Presentation:
Smith, HJ. (April 2016). *The ethical implications and religious significance of organ transplantation payment systems*. Poster presented at: Tulane Delta Omega Society Poster Symposium; New Orleans, LA.

- **Tulane Community Health Research** Sep 2013 – May 2016
 - *Student-Faculty-Community Partnership for Low-Cost Primary Care Clinic in New Orleans*
 - Poster Presentation:
Arno, ST, Flowers, TS, Crowther, JE, Ockenfels, B, Roth, A, **Smith, HJ**, McConville, JB, Mohiuddin, A, & Andrews, J. (May 2016). *Student-faculty-community partnership for low-cost primary care clinic in New Orleans*. Poster presented at: Louisiana State University Health Regional Research Day; Baton Rouge, LA.

- **Medical Ethics Education Research** Jun 2014 – Dec 2016
 - *Defining and Achieving the Goals of Medical Ethics Education*
 - Poster Presentation:
Smith, HJ. (May 2016). *Defining and achieving the goals of medical ethics education*. Poster presented at: Tulane Health Sciences Teaching Scholars Education Symposium; New Orleans, LA.

- **Undergraduate Research** May 2010 – Aug 2011
 - *Aerosolization of Bacteria Caused by Pulsatile Lavage Wound Treatment*
 - Performed bacterial culturing of wound treatment facilities. Conducted on behalf of the Infection Control and Epidemiology department for Lee Memorial Health System.

- **High School Research** May 2007 – Apr 2009
 - *A Cross-Sectional Study of Methicillin-Resistant Staphylococcus aureus Colonization of Pet Therapy Dogs*

- Intel International Science and Engineering Fair (2009)
- *Methicillin-Resistant Staphylococcus aureus in Veterinary Personnel and Their Pets*
 - Young Epidemiology Scholars (YES) Competition – National Finals (2008)

U.S. ARMY EXPERIENCE

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|--|--|
| <ul style="list-style-type: none"> ● General Preventive Medicine Residency, PGY-2 & 3 <ul style="list-style-type: none"> ○ Uniformed Services University, Bethesda, MD ● Certificate in General Preventive Medicine <ul style="list-style-type: none"> ○ Uniformed Services University, Bethesda, MD ● Certificate in Clinical Tropical Medicine and Travelers' Health <ul style="list-style-type: none"> ○ Uniformed Services University, Bethesda, MD ● Transitional Year Internship, PGY-1 <ul style="list-style-type: none"> ○ Tripler Army Medical Center, Honolulu, HI ● Combat Casualty Care Course (C4) <ul style="list-style-type: none"> ○ Fort Sam Houston, TX ● Officer Promotion to Captain <ul style="list-style-type: none"> ○ National World War II Museum, New Orleans, LA ● Internal Medicine Sub-Internship <ul style="list-style-type: none"> ○ Tripler Army Medical Center, Honolulu, HI ● Preventive Medicine Sub-Internship <ul style="list-style-type: none"> ○ Walter Reed Army Institute of Research, Silver Spring, MD ○ WRAIR-GEIS Operational Clinical Infectious Disease Course (Aug 2016) ● Basic Officer Leadership Course (BOLC) <ul style="list-style-type: none"> ○ Fort Sam Houston, TX ○ U.S. Army Certificate of Achievement (Jul 2014) ● Officer Commission as 2nd Lieutenant <ul style="list-style-type: none"> ○ New Orleans, LA | <p>Jul 2018 – July 2020</p> <p>Jul 2018 – May 2019</p> <p>Feb 2019 – May 2019</p> <p>Jun 2017 – Jun 2018</p> <p>Apr 2018 – May 2018</p> <p>May 2017</p> <p>Oct 2016 – Nov 2016</p> <p>Aug 2016 – Sep 2016</p> <p>Jun 2014 – Jul 2014</p> <p>Jan 2013</p> |
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PROFESSIONAL ORGANIZATIONS

- | | |
|---|---|
| <ul style="list-style-type: none"> ● Member of the American Medical Association (AMA) ● Member of the Association of Military Surgeons of the United States (AMSUS) | <p>2013-Present</p> <p>2013-Present</p> |
|---|---|

- Member of the American College of Preventive Medicine (ACPM)

2015-Present

HOBBIES & INTERESTS

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|--------------|-------------------------------------|
| ● Basketball | ● Pre-Columbian art and archaeology |
| ● Philosophy | ● Green Bay Packers part-owner |